ITEM No. 24
FILE No. XXIII—23

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PHARMACEUTICALS AND INSECTICIDES
I.G. FARBENINDUSTRIE A.G., HOCHST/MAIN

COMBINED INTELLIGENCE OBJECTIVES
SUB-COMMITTEE

CONFIDENTIAL

PHARMACEUTICALS AND INSECTICIDES AT THE I.G. FARBENINDUSTRIE PLANT HOCHST A. MAIN

10 - 11 April 1945

Reported By

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CIOS Target Number 24/4

COMBINED INTELLIGENCE OBJECTIVES SUB-COMMITTEE
G-2 Division, SHAEF (Rear) APO 413

CONFIDENTIAL

T A B L E O F C O N T E N T S

Composition of Team.

(Note: Members actually engaged in the investigation of this target are indicated by an asterisk in the list on page 1).

1. Introduction. C O N F I D E N T I A L

This target is a large one, involving both industrial chemicals and pharmaceuticals, and the two day period available to our team permitted interrogation relating to only a small portion of their activities.

The Hoechst plant normally employed up to 12,000 persons. Near the end of the war they had 9,000 employees, of whom 2,900 were civilian Russian, French, Polish, and other displaced persons. The plant was practically untouched by bombs, but due to lack of power, operations had almost ceased beginning in January, 1945.

Normally, one third of the Hoechst output value was represented by pharmaceuticals, requiring about 1400 workers. Their other activities were in the fields of dyes, alkalis, mineral acids, solvents derived from acetylene, plasticizers, color fixatives, glycerol, building material products, and vinyl plastics. Prof. Lautenschlaeger, the general Director, stated that the most important progress and research during the war was in the field of pharmaceutical products, including compounds to combat colds and typhus; and vaccines, hormones, vitamins, antibacterial agents, and synthetic drugs. They had also done considerable work on nitro compounds to be used in explosives, but this phase was not gone into further.

Hoechst has a large department for making packaged pharmaceutical products, such as tablets, ampoules, etc.

The firm appears to have been well organized and capably managed by Prof. Lautenschlaeger and his staff. Our C.I.O.S. team was well received and we were given satisfactory cooperation in our interrogations. Lautenschlaeger is tall, dignified, correct, and somewhat austere; his associates, Bockmuehl, Fussgänger, Schaumann, Fehrle and others were more ready to volunteer information. Naturally, the principal concern of the entire staff was to obtain permission to resume operations, and to protect the physical plant from feared depredations and vandalism by displaced persons.

2. Personnel.

An organization chart of the Hoechst scientific personnel is attached as Appendix I.

3. Pharmaceuticals.

A complete list of the Hoechst Pharmaceuticals and insecticides is given in Appendix B.

a. Chemotherapy of Infection and Neoplastic Diseases.

(1) General Remarks.

Studies on the chemotherapy of virus and rickettsial diseases at I.G. Höchst are carried out under the direction of Dr. R. Fussgänger, chief of chemotherapy. Fussgänger's earlier work had to do with the chemical structure and synthesis of hormones. He was assigned to his present position several years ago when the former chief of chemotherapy resigned, presumably because he was of Jewish extraction. Fussgänger is intelligent and conversant with the literature in the field of infectious diseases; he was cooperative during the visit of the CIOS team..

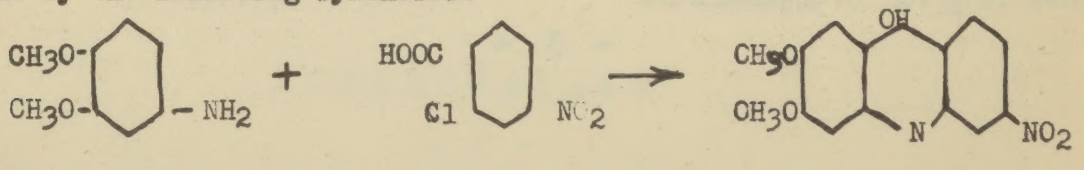
The general plan for the study of chemotherapeutic agents is the same at Fussgänger's laboratory in Höchst as it is at Kikuth's laboratory at Elberfeld. (See report of CIOS Team No. 110. on I.G. Elberfeld and Leverkusen). Various compounds prepared in different divisions of I.G. are submitted to the chemotherapy laboratory for testing. After the toxicity of the substances has been determined they are tested for their effectiveness against a number of infectious and neoplastic diseases. Among the experimental virus diseases which are employed regularly in the testing of new drugs at Höchst are influenza A.,louping ill,lymphogranulona venereum; all the work is done in mice. Murine typhus is the only example of the rickettsial virus used in chemotherapeutic trials; mice are infected intraperitoneally in these studies. Tumors employed in the experimental set ups are the Broun - Pearce tumor, a sarcoma of rats, a fowl sarcoma, and occasionally the Shope papilloma. Several types of trypanosomal infections in mice are also used in the testing.

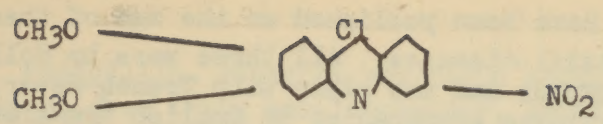
Many types of compounds are run through the gamut of biological tests; however, no sulfa compounds are studied at Höchst; these are all studied at Elberfeld.

None of the studies at Höchst on virus and neoplastic diseases have revealed new substances of chemotherapeutic value. Certain of the more interesting findings in other infectious diseases are summarized in the following paragraphs.

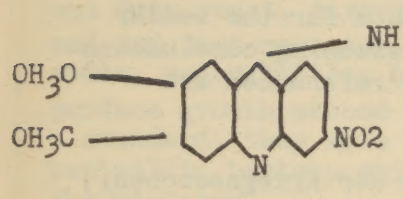
Chemotherapeutic studies have gradually lessened during the past few years and during the last six months have almost ceased because of the shortage of animals.

(2) Nitroacridine and Rutenol. Of the many compounds studied for the treatment of murine typhus, the only ones stated to have shown promise is nitroacridine, or mixtures containing this compound. It is made by the following synthesis:





H2N CH2 CH OH CH2 N(C2H5)



Nitroacridine.

The nitroacridine itself is not a new compound. The series of which it is a member was originally used against streptococci and staphylococci. It was found that the acridine nucleus and the nitro group are necessary for effectiveness against typhus. The compound has been tested clinically in about 200 cases of R. mooseri. It is given orally and intravenously. The latter mode of administration causes some sclerosis of veins and oral administration causes vomiting, hence it is administered in divided doses. In 20-gram mice, the effective dose was found to be 3.3 to 5 mg.

Rutenol. is the name of the pharmaceutical product of 2 parts of nitroacridine plus 3 parts of arsenic trioxide, which forms a salt. A synergistic effect is claimed. Rutenol granulata contains 5% of this active material. Fussgänger has not published his perimental data on this subject. However, in accordance with I.G. policy he prepared a prospectus on nitroacridin and on rutenol summarizing the available information. Such a prospectus is given to those clinicians who intend to subject I.G. drugs to clinical trial. Translations of Fussgänger's articles on nitroacridin and Rutenol are presented in Appendices 3 and 4. These data are quite convincing, (see charts in appendices dealing with mortality curves of treated and control mice). Examination of a large number of Fussgänger's protocols and summaries leads one to the conclusion that the examples chosen for illustration in his article are representative of the general experiences. The experiments are not reproducable with complete regularity, however, apparently because of two variables which Fussgänger did not control adequately. These were variations in the infectivity of the innoculum and use of different strains of a suspension which contained a known number of minimal lethal doses of the infectious agent. Mice used in these experiments were obtained from different breeders. Mice from one of these breeders consistenly failed to survive infection when tested with amounts of the drugs which were adequate to protect the majority of mice supplied by another breeder.

Guinea pigs infected with epidemic typhus richettsiae and treated with nitroacridin developed fever in the same way as untreated controls. The drugs have not been tried in amimals injected with rickettsiae of Spotted Fever, Boutonneuse Fever or Scrub typhus

Only three reports have been published on the use of these drugs on patients with rickettsial diseases. All three were by Holler; two deal with epidemic typhus and the other with Trench Fever. Photostats of the original articles accompanied by English translations are filed with the Secretariat. These reports are of little or no scientific value since they present inadequate data for the reader to decide whether the author's contraditory and sweeping conclusions have any foundation in fact. For the record the references are as follows.

(1) Kasuistiche Beiträge zur Therapie der Kriegsseuchen, Holler, G., Mathis A., and Ortner, E., Wiener Klin. Woch. 1944, 27-28, 345.

(2) Eine sehr erfolgreich streng kausalpathogenetisch eingestellte Therapie des Fleckfiebers, Holler, G., and Zajitschck, R. Med. Klinik, 1944. 17-18, 247

(3) Welche Erfahrungen liegen bei der Behandlung des Wolhynienfiebers vor? Holler, G., Med Klinik 1944, 25 374.

In view of the good chemotherapeutic results obtained with nitroacridin and Rutenol in experimental murine typhus injection in mice it appears worthwhile to extend the studies on this group of drugs to determine their effects on other experimental ricksettsial infections, notably scrub typhus. It also appears desirable to obtain accurate information on the usefulness of this drug in epidemic typhus in human beings.

Samples of Nitroacridin and Rutenol (active materials) and Rutenol granulosa (5% active material) are filed with the Secretariat.

Informant Dr. R. Fussgänger.

(3) Congasin and Preparation 7602

These compounds which are related to Surfen and have a typanosomidal action are still considered of interest by Fussgänger. Little or no experimental work has been done with them in the past three years. Reports entitled "Congasin," Fussgänger, R. Sonderdruck aus Medizin u Chemic Bd IV. 1942 and "Die Behandlung der akuten Chagas - krankheit mit 7602 (AC) Bayer," Mazza, S., Deutsche. Trop Med.Zeit.1941, 45 577 are filed with the Secretariat. Stitts Diagnosis, Prevention and Treatment of Tropical Disease 6th Edition 1943 discusses these drugs with comparatively little enthusiasm.

(4) Preparation 9659a (Bismuth salt of glycolylaminophenyl arsenic acid)

This bismuth-arsenic combination has been reported to be of value in the treatment of patients with amebic dysentery. The drug is discussed at length in the report of CIOS Team 110 on I.G. Elberfeld and Leverkusen.

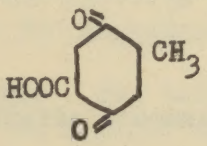
(5) Penicillin research was begun about two years previously using strains from their own laboratory, and also one obtained from Euler in Sweden. None was particularly good. The best culture medium was from yeast, also whey. They used the surface method in flasks, and had just recently begun submerged growth experiments on a small scale, using bottles holding about 3 gallons. Their capacity by the surface growth method was 7½ million Oxford units per month. As a standard, they were employing a package of captured Burroughs-Wellcome penicillin tablets which had been turned over to them by the German War Ministry.

A batch was considered to be 300 liters of harvest. Butyl alcohol was used for extraction. The butyl alcohol extract was concentrated by distillation, and after further processing to get it into ether solution, the latter was twice chromatographed, giving a 60% overall recovery. The product was dried from the frozen state and was brown in color, with a potency they believed to be about 150 Oxford units per milligram. None of this product was supplied to the German Army; most of it was intended for structural investigations, and for experiments on stabilization. Dr. Wegmann, in charge of this work, stated that they had not done any appreciable amount of structural research, as their product was too impure.

The Höchst penicillin operations may be summarized as follows:

1 liter of harvest = 256,000 dilution units
Ratio of dilution units to Oxford units = 25:1.
256,000 dilution units = approx. 10,000 Oxford units.
Loss in operation = about 5,000 Oxford units.
Production per month = 1500 liters of harvest
= 7,500,000 Oxford units
= 200 million dilution units.

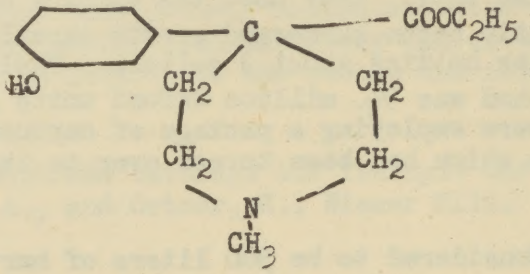
Each dry ampoule = 15 mg. = 2000 Oxford units of sodium salt.

Höchst has not worked much on other antibiotics. They studied quinones of the type 

, but found none having activity comparable to penicillin.

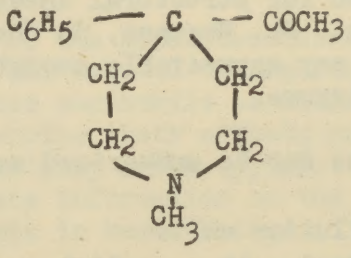
b. Analgesics Dolantin was made at the rate of 200 to 300 kg. per month.

Dr. Bockmühl stated that considerable research has been carried on in this field. The meta-hydroxy derivative, which was made by analogy to morphine, is



This compound is more powerful than Dolantin. The corresponding ortho and para - hydroxy compounds are not efficient analgesics.

The compound



was stated by Bockmühl to be 3 times as effective as Dolantin. The corresponding ethyl analog is still better. This series is being tested clinically.

By analogy to Trasentin,

$$(C_6H_5)_2\ CH\ COOC_2H_4\ N(C_2H_5)_2$$

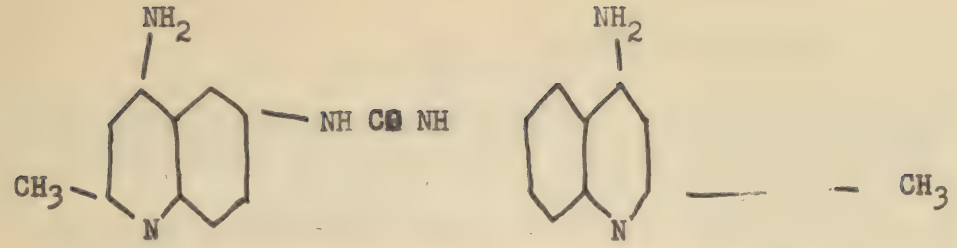
they prepared

$$(C_6H_5)_2\ C(CH_2CH_2N(C_2H_5)_2) - COOC_2H_5$$

which has both analgesic and contispasmodic effects.

* c. Pyramidon is manufactured in a large plant, with a capacity of 540 metric tons per year. In 1938 their production was 200 tons. It was stated that Germany produces 2 trillion Pyramidon tablets annually, and that practically no agranulocytosis is encountered. Combinations containing Pyramidon are also extensively employed.

* d. Rivanol is manufactured in quantity for wound disinfection. A newer product, about ten years old, is Surfen,



It is a colorless substitute for Rivanol, used as a wound antiseptic and gargle.

* e. Vitamins. Ascorbic Acid output at Höchst was 12,000 kg. per year. Vitamin E was made solely by the extraction of wheat germ, and it had a good market. Synthetic Vitamin K was also manufactured. Experimental work was under way to develop an oil solution for injection. Höchst made no B vitamins, nor vitamin A.

* f. Salvarsans. No unusual methods of manufacture appeared to be involved. The filled ampoules were evacuated from a vacuum line manifold; the vacuum line contained a Geisler tube to indicate by color the degree of vacuum. A. Tecla Field was used for the final vacuum inspection of the ampoules.

The salvarsan base is made in wooden kettles, and silver lined kettles are used for the preparation of the hydrochloride salts.

* g. Novocaine is made by condensing ethyl p - aminobenzoate with diethyl - aminoethanol at 150°C. in the presence of sodium. An 80% yield is obtained. Novocaine solution for sale are made as follows: A sodium chloride solution is made in a closed vessel under hydrogen; this solution is filtered into a closed porcelain vessel of about 20 gallon capacity, using a closed system. This solution is forced through a glass tube containing the required amount of crystalline Novocaine and epinephrine. Filling into ampoules is done in a closed system, using alternate vacuum and hydrogen pressure; no preservative is used in the solution.

* h. Analeptics were not made by Höchst. It was stated that Amphetamine, Neospiran and Pervitin were not extensively used in Germany, except perhaps for Amphetamine in aviation.

* i. Enteric Coatings for tablets are made from polysterol maleic acid anhydride, and applied as a 7% acetone solution.

* j. Suppository Base called "Postonal" is polyethylene oxide, to be used in place of cocoa butter. It does not melt at body temperature but is soluble in water.

* k. Antispasmodics. Aspasan is a new product, synthesized as follows:

$(C_6H_5)_2CH\ CN + Cl\ CH_2CH_2N(C_2H_5)_2 \xrightarrow{NaNH_2}$

CN

$(C_6H_5)_2C-CH_2CH_2\ N(C_2H_5)_2$. This intermediate is isolated, then treated with excess sodamide, whereby the CN group is removed and replaced by H, to give Aspasan, $(C_6H_5)_2\ CH\ CH_2C_2N(C_2H_5)_2$. Aspasaniis marketed in combination with dihydroxy-ephedrine and monohydroxyephedrine (Suprafen).

* l Hypnotics These are made at Elberfeld. Formerly Novonal (diethylallytacetannid) and Nirvanol were manufactured at Höchst, but they are no longer being produced.

No digitalis or strophanthus preparations are made.

* m Manufacturing methods.

Manufacturing directions for the following products were obtained and have been given to the Secretariat: Penicillin, Dolantin, Nitroacridin (No. 3582), Novalgin, Novocain Pantocain, Preloban, Progesterone, Cortenil, Pyramidon, Racedrin, Rivanol, Salyrgan, and Suprarenin.

* n Recommendations. This is one of the most outstanding drug and chemical units in Germany, and merits much more detailed study than this C.I.O.S. team was able to devote to it in the two days we had available. It is therefore recommended that a qualified pharmaceutical team be assigned for a further and more intensive study.

Interviewed:

Drs. Lautenschläger, Max Bockmuehl, R. Fussgänger, Schaumann, Alfred Fehrle (pharmaceutical manufacturing), Wegmann, and Stephan.

A P P E N D I X 1

Professor Dr. Lautenschläger - General Director of the Entire Plant and Director of the Pharmaceutical Division.

Dr. Dr. M. Bockmühl - Director of the Research Pharmaceutial Division.

a. Dr. G. Ehrhart - Director of the Laboratory for Drug Synthesis.

Dr. E. Bartholomäus	Dr. W. Krohs
Dr. C. Eislob	Dr. H. Loditschko
Dr. L. Stein	Dr. W. Aumüller
Dr. H. Jonsch	Dr. W. Schneider
Dr. H. Ruschig	Dr. H. Pötz
Dr. P. Hartmann	Dr. W. Persch
Dr. A. Schmidt	

b. Dr. W. Ludwig - Director of the Biochemical Laboratory.

Dr. F. Lindnor	
Dr. H. Coppinger	Dr.Th.Wegmann
Dr. A. Magor	Dr. H. Vetter

c. Dr. O. Schaumann - Dozent in the University of Frankfurt/Main and Director of the Pharmacological and Physiocological Laboratories.

Pharmacist Eug. Dörzbach	
Dr. R. Rigler	Dr. H. Boucholt

d. Dr. O. Wagner - Dozent in the University of Giessen and Director of the Parasitological Laboratory.

Dr. W. Hohorst

e. Dr. R. Fussgänger - Director of the Chemotherapeutic Laboratory.

f. Dr. J. Stephan - Director of the Sero-bacteriological Laboratory.

g. Dr. K. Pfaff - Director of the Laboratory for Plant Protection.

Dr. M. Erlenbach	Dr. W. Staudermann
Dr. W. Finkenbrink	(Botanist)
(Entomologist)	Dr. W. Gelmroth

h. Dr. W. Hermann - Director of the Salvarson Laboratory

Dr. Fr. Hampe	Dr. Hilmer

i. Apoth. L. Middendorf - Director of the Galenical Laboratory.

j. Dr. J. Eisenbrand - Director of the Pharmaceutical-analytical Research Laboratory including physical methods.

Apoth. Sionz
Dr. Picher

Dr. J. Eisenbrand

k. Dr. J. Weber - Director of the Scientific Bureau
Dr. Köpp
Apothekor Fischmann

Frankfurt a/Main-Hoechst
den 4 April 1945/G

APPENDIX 2

List of the Pharmaceutical Remedies of the I.G. Works, Höchst

1. Remedies for Human Use
   a. Anaesthetics
      Anaesthesin
      Novocain
      Novocain-Corbasil
      Nosuprin (local-anaesthetic for dentistry)
      Pantocain
      Impletol (complex combination of Novocain and Caffeine)
   b. Sedatives
      (1) Antipyretics, Antirheumatics and Antiarthritics
      Antipyrin
      Migränin
      Melubrin, Novalgin
      Cardan (Novalgin-Pyramidon) Pyrazolon-group
      Novalgin-Quinine
      Pyramidon
      Trigemin (Pyramidon+Butylchloralhydrate)
      Hexophan (combination of quinoline and carboxylic acid)
      (2) Analgesics and Spasmolytics
      Dolantin
      Aspasan (remedy for asthma)
   c. Hormon-Preparations
      Lutren (Corpus-luteum-hormon)
      Cortenil (synthetic cortical-hormon)
      Corteniletten
      Suprarenin (synthetic hormon of suprarenal gland)
      Elityran (preparation of the thyroid gland)
      Elityran K (a substance having the action of the thyroid gland and made of non-specific albumen by iodation).
      Emanal (a preparation of the thyroid gland, enriched with iodine).
      Erugon (testical-hormon-preparation)
      Festal (pancreas-enzyme-preparation with hemicellulase)
      Hypophysin (labour-exciting drug and tonic of the vessels)
      Iliren (an Adrenalin-free preparation of the suprarenal cortex)
      Orasthin (a constituent of the posterior lobe of the pituitary gland, with a specific action on the uterus)

Prelobam (active principle of the posterior pituitary lobe)
Tonephin (a hormon of the pituitary gland (pars posterior) acting as a tonic on the intestine and checking diuresis).
Torantil (obtained from the intestinal mucrous membrane and possessing anti-allergic and detoxicating properties).
Insulin (Normal - Insulin
(Depot - Insulin, turbid
(" " clear
(Native - Insulin
Lacarnol (a nucleoside preparation acting on the circulation).

d. Vitamins
Cantan (Vitamin C)
Citrin (permeability-Vitamin, factor P)
Hemodal (Vitamin K-Preparation)
Priovit (water-soluble vitamins of the B and C-group)
Ereton (natural Vitamin E-preparation).

e. Chemotherapeutical and Antiseptical Remedies
(1) Metal-combinations
Casbis (a bismuth preparation for injections)
Ebesal (organo-copper combination for combating tuberculosis).
Lopion (organo-gold combination for combating tuberculosis).
Salyrgan (organo-mercury combination
(2) Non-metal-combinations
Trypeflavin (antiseptic for treating wounds, antigonorrhoic and internal chemotherapeutic)
Trypaflavetten
Pan-flavin-pastils
Surfen (a colorless chemical substance for use in surface and deep antisepsis).
Surfen-preparations: Revasa-Tablets.
Rivanol (a specific for use in deep and surface antisepsis).
Rivanol-preparations: Rivanol granulate
Rivanoletten
(3) Arsenic preparations
Salvarsan
Salvarsan-Sodium
Myosalvarsan
Neosalvarsan
Neo-Silbersalvarsan
Solu-Salvarsan
Spirocid (a compound of arsonic acid).

f. Synthetics acting on the circulation
Icoral (circulatory and respiratory restorative)

Racedrin (Raceme-Ephedrine)
Rephrin (Racedrin + Raceme-Suprarenin)
Suprarenin (compare Hormon-preparations)
Suprifen (a circulatory tonic and antileptic)

g. Stomachics
Hydronal (The antacid for conditions of gastric irritation and disorders of secretion).
Orexin (for improving the secretion of the gastric juice).

h. Narcotics
Solaesthin (inhalation anesthesia)
Stickoxydul (narcotic gas)

i. Eczema Remedies
Pellidol, in form of: Pellidol ointment,
Pellidol bougies
Tumenol-Ammonium (an antiphlogistic dermatological preparation)

j. Remedies for indications not enumerated in a. - i.
(1) Synthetics
Lubisan (anthelmintic)
Sajodin
Sajodinetten (a lipotropic iodine preparation)
Salyrgan (organo-mercury-combination, diuretic)
Varon (labour exciting drug)
Tonophosphan (for assisting metabolism)
(2) Biochemical Remedies
Devegan (for the treatment of loucorrhoea)

k. Others
Postonal (ground-mass for suppositories)
Ninhydrin (diagnostic)

21 April 1945/G

Sera and Vaccines

Anti-cholera Vaccine
Anti-Dysenteria-Polyfagin
Febris-Undulans Vaccine of "Behringwerke"
Gonargin (Gonococcus Vaccine)
Mixed Gonorrheal Vaccine Behringwerke
Anti-Influenza Vaccine Mixed Behringwerke
Gripcaline-drops (mixture of antigens for the early therapy and prophylaxis of influenza)
Anti-catarrh Vaccine and Mixed Behringwerke
Anti-whooping cough-Vaccine Behringwerke
Leukogen (antistaphylococcic Vaccine)
Omnadin (an non-specific Vaccine)
Paragen (immune therapeutic)
Anti-whooping cough Vaccine Mixed Behringwerke

Phytossan (monovalent antiwhooping cough Vaccine)
Anti-Pneumococcic Vaccine Behringwerke
Anti-Streptococcic and Anti-Staphylococcic Vaccine Mixed Behringwerke
Tetra-Vaccine Behringwerke (a mixed Vaccine of Typhoid, paratyphoid and cholera A + B Bacilli).
Trichophytin (a polyvalent extract prepared from trichophyton fungus.
Tuberculin-Preparations
Anti-Typhoid Vaccine Behringwerke
Anti-Typhoid and Anti-paratyphoid Vaccine T.A.B. Behringwerke
Typhoral (a polyvalent antityphoid Vaccine)
Anti-typhoid - Anti-paratyphoid B Polyfegin
Dermotubin (a skin-tuberculin).

2. Remedies for Veterinary-Medical Use

a. Anaesthetics
Anaesthesin
Novocain
Novocain-Suprarenin (local anaesthetic)
Pantocain (surface anaesthetic)

b. Analgesics and Antispasmodics
Novalgin

c. Hormone Preparations
Elityran (preparation of the thyroid gland)
Erugon (testical hormon preparation)
Festal (pancreas-enzyme preparation with hemi-cellulase)
Hypophysin
Insulin
Orasthin (a constituent of the posterior lobe of the pituitary gland, with a specific action on the uterus)
Suprarenin (synthetic hormon of suprerenal gland)

d. Vitamins
Eviabit (oil from wheat germ with standardized Vitamin-E content)
Cantan (Vitamin C)

e. Chemotherapeutical and antiseptical Remedies
Methylene-blue medicinal "Bayer"
Methyl-violet medicinal "Bayer"
Trypanblue (Specific for various kinds of piroplasmosis)
Bovoflavin ointment (incubation infection of the female and male cattle)
Congasin (for combating diseases in cattle and horses caused by Tryp. congolense and Tryp. vivax)
Entozon-Granulate (chemotherapeutical soothing antiseptic)
Entozon-rods
Entozon-studs
Entozon-ointment

Rivanol (a chemotherapeutic for use in surface and deep antisepsis)
Trypaflavin
Neosalvarsan
Spirocid-Sodium (for spirochaetosis of fowl and others)
Natrolets (a disinfecting of virus)
Osmaron (disinfecting and sliding agent to be used in milking - germicidal)

f. Synthetics acting on the circulation
Rephrin (Raceme Ephedrin)(and Raceme-Suprarenin).
Suprarenin (compare Hormone preparations)

g. Anthelmintics and other effective remedies for combating intestinal parasites
Allegan-plates (anthelmintic and roborant)
Avomin (anthelmintic)
Ciff-capsules (Anthelmintic)
Nemural (anthelmintic)
Igitol-powder and pills (for treatment of liver-rot)

h. Remedies for combating ectoparasites, horn-flies and others
Malix (Dusting powder obtained from derris)
Derrophen (a preparation obtained from derris and to be used for combating larvae of horn-flies on cattle, scab, mange, vermin, Herpes tonsurans in cattle and horses)

i. Others
Pellidol ointment (used to promote epitheliation)
Salyrgan (a diuretic)
Tonophosphan-Solution (for assisting metabolism)

21 April 1945/G

Sera and Vaccines (for veterinary use)

Amblosin (Bang's bacillus of abortion)
Antidiplococcic and Formol-Vaccine Behringwerke
Druse Vaccine Behringwerke
Fowl-Cholera Vaccine Behringwerke
Fowl-Diphtheria and smallpox Vaccine Behringwerke
Mixed Vaccine Behringwerke for Paralysis of foals
Omnadin
Mother Vaccine Behringwerke
Pig Paratyphoid Vaccine Behringwerke
Pneumonia Vaccine Behringwerke
Pullorum-Antigen Behringwerke
Anti-streptococcic Vaccine Behringwerke for veterinary use
Tuberculins (Old Tuberculin, Bovine Tuberculin, Tuberculin-Diagnostic for ophthalmic reaction)

List of Commercial Products of the Fungicide and Insecticide Department of the I. G. Works, Hoechst

Tritisan - a dry seed dressing free from metals for the treatment of Bunt or Stinking Smut in Wheat
Vitigran - a fungicide containing copper oxide and having a particularly good adherence
2317 W - a fungicide free from metals against Peronospora
Nosprasit - the cuprous and arsenical fungicide and insecticide for the simultaneous treatment of fungus and insect pests in fruit culture.
Bulbosan - to cure brown patch disease of tomatoes
Brassisan - against Plasmodiophora brassicae
Brassicol - against botrytis (sclerotinia)
Nirosan-Spraying Agent-Free from Arsenic) against Clysia
Nirosan Dust) ambiguella and Polychrosis botrana
Copper Nirosan Spraying Agent) for the simultaneous treatment
Copper Nirosan Dust) of Peronospora and Clysia ambiguella and Polychrosis botrana
Aresin - against Leptinotarsa decemlineata
Gralit - dusting agent against eating insects
Nicropren new - a nicotine-saving product against sucking insects
Gix - against flies
Dizan - an insecticide against cockroaches
Grodyl new - a spray against Calandra granaria
Synthetic caterpillar lime Hoechst - against all creeping insects
Agrotin - a product for improving the wetting power of fungicides

APPENDIX 3

Nitroacridine preparation 3582 (Chemisch-Pharmazeutische und Sero-Bakteriologische Abteilung, I.G. Farbenindustrie A.G., Frankfurt/Main - Höchst - R. Fussgänger)

Chemotherapeutic remedies for true typhus with specific efficacy have not been known until this time. During the last ten years systematic experiments to find such remedies have been undertaken. Otto, Wohlrab, and Schäfer especially have worked out extensive experimental series, but it has never been possible to determine anything more than mere traces of an influence upon the disease in mice. As a causative agent, these investigators used a rickettsia strain, isolated by Mooser, of Mexican typhus (tarbadillo fever), on whose suitability for chemotherapeutic experimental series Wohlrab reported in Berlin in 1937 at the 17th congress of the Vereingung für Mikrobiologie.

The danger of an increased incidence of typhus, caused by the Eastern Campaign, caused the author to initiate very extensive laboratory tests in quest of a chemotherapeutic substance for medicinal therapy of typhus, since the manufacture of vaccines in quantities required for protective inoculation of the entire military and civilian personnel in the Eastern area cannot be carried through even with the best type of organization.

Since work with the causative agent of true typhus in large experimental series is difficult and since the study of immunity conditions showed the close relationship of genuine typhus with the causative agent of Mexican typhus, the chemotherapeutic test series were performed with Mooser's strain. Extraordinarily many preparations from a multiplicity of chemical groups were tested for their efficacy by means of this model test. Above all many of the classical chemotherapeutic remedies were examined; in most cases they proved to be totally ineffective. Certain indications of an effect were found in oral administration of some arsenic acids. In the further course of these large-scale experiments a substance was found which has a very regular, strong influence upon the course of the disease in regard to intensity and lethal outcome, and in experimental animals were kept alive and were cured. This substance is No. 3582 in extensive clinical tests in genuine typhus, Volhynian fever, and other rickettsioses. It is a nitroacridine derivate of complicated structure, and it is readily soluble in water.

Toxicological data

The toxicity of the substance is but slight. The maximum tolerated dose is in the mouse (per kg) 0.15 gm in subcutaneous and 0.5 gm in oral administration. Rabbits tolerate intravenously 25 mg per kg. In the animal experiment, No. 3582 never showed any recognizable injury of the gastric and intestinal mucosae even in great overdosage.

For biological tests of the new typhus remedy on the causative agent of Mexican or murine typhus, mice were used in large test series, as experience had shown that uniform results can only be obtained if each preparation, each individual dosage, and each manner of administration (subcutaneous, oral, intravenous) are applied to as large a group of mice as possible, in order to reduce the giological stray results occurring in this infection to a minimum. For the infection of the series of mice, the author used the emulsified brains from gravely diseased passage animals, in certain dilutions, which caused an 80 - 100% mortality in the untreated control animals. In spite of frequent adjustment of the optimal dilution of the emulsified brains there appear fluctuations in virulence, evidently of seasonal causation, of the causative agent, which render the determination of effective remedies difficult. After substance No. 3582 had excelled time and again in all tests, the author began in all large-scale tests to treat a collective group with this substance, in addition to the untreated control animals, and thus he was able to determine the degree of efficacy of a new substance in comparison with No. 3582 as a standard substance.

The aspect of the disease in intraperitoneally infected mice had approximately the following course: On the 4th or 5th day after infection the first symptoms of the disease became visible. They were a lack of motion and raised fur; as the disease continued, there appeared uni- or bilateral conjunctivities, and extensive edemas developed in the head of the animal. Before death occurred -- generally between the 8th and the 10th day of the test -- the author observed occasionally symptoms of paralysis, and frequently diarrhea and spasms. While the mice in the control series had, with very few exceptions, died by the end of the 10th day of the test, the disease in the majority of the animals treated with substance No. 3582 orally had a distinctly milder course. In most instances these animals did not even show any symptoms while the control animals already displayed very grave symptoms of disease. Lack of motion and raised fur appeared several days later. Many mice recovered very

rapidly from this condition. Only a part of the experimental animals succumbed to the infection, however much later than the control animals.

From a juxtaposition of the percentages of the mice surviving every day of the experiment it was possible to obtain a standard for determining the efficacy of a preparation. The best result was obtained by oral administration of No. 3582 for a period of several days. The greatest number of survival were obtained with 5 times 5 mg per 20 gm mouse, administered orally. With smaller daily doses the effect was smaller, likewise the substance appeared less effective in subcutaneous and intraperitoneal application, evidently because of the greater toxic effect in this type of application.

The use of No. 3582 as standard substance in almost all test series made it possible to calculate the average course of the disease in treated and untreated mice from a very large number of experimental animals, and to present it in an unequivocal curve. In this the control animals participating in the same large-scale experiment were contrasted with the series treated with substance No. 3582. The following curve I is based on 8 experimental series with 79 treated and 150 untreated mice. The form of the course presented in curve II --untreated control animals infected with rickettsia -- represents an average of 675 infected mice. In juxtaposition to this is the curve of 555 mice which all had received orally the standard dose of 4, mostly 5 times 5 mg of substance No. 3582. While of the control animals only 8.4% had survived the infection at the end of the 17th day of the test, in 31 large-scale experiments with No. 3582 an average of 58% of the experimental animals had survived, in spite of the fluctuations in virulence. Extension of the period of observation hardly changes this quotient at all; on the other hand the juxtaposition of the two curves shows that a premature interruption of the experiment on about the 10th or 11th day and an evaluation based thereon causes an overestimation of the efficacy of the substances tested. Ultimately, curve III represents the result of 70 experimental series, in which 1234 mice had received the standard dose of 5 times 5 mg substance No. 3582 orally and in which 1267 mice had been infected as control animals, without receiving any treatment. In spite of the fluctuating virulence of the causative agent, an average of 58% of the animals treated with No. 3582 survived, whereas only 19% of the control animals survived. Extending the period of obser-

vation does not change the curves in any appreciable manner.

Experiences lasting more than one year have taught that the percentage of mice surviving after treatment with No. 3582 fluctuates according to the virulence of the rickettsia; i.e., when the virulence was high, all control animals died rapidly, and only a small percentage of the 3582-treated mice remained alive. If, on the other hand, virulence was low and 20-30% of the control animals remained alive, up to 100% of the 3582-treated animals survived. There always was a certain distance between the two curves, which enabled the author to establish an efficacy quotient. If I represents the percentage of surviving animals after treatment, and II represents the percentage of surviving control animals, based on the animals at the beginning of the test, the efficacy quotient, i.e., the percentual number of the mice which is preserved alive by chemotherapeutic treatment after subtraction of the control animals, is calculated from the formula:

$$Q = \frac{I - II}{100 - II} \cdot 100$$

Application of this formula yields from curve II an efficacy quotient of 47.6% and from curve III an efficacy quotient of 48.2%. In spite of great fluctuations of virulence this efficacy quotient thus remained almost unchanged in the two halves of the year.

Tested in the same manner, Rivanol, Trypaflavin, Atabrine, and numerous other chemotherapeutics proved ineffective. The fact that after treatment with substance No. 3582, on basis of the large amount of experimental material at hand more than 48% (after subtraction of the surviving control animals) were cured represents a great success in view of the fact that most of the chemotherapeutic tests always had negative results. This success justifies clinical tests of applying the substance in true typhus. These tests are even more justified as it is known from other chemotherapeutic model tests that even a delay of the course of the disease in the animal may be considered as an indication for good chemotherapeutic efficacy in the human organism.

Studies on the clarification of the mode of action of the substance are in progress. One must assume that the preparation changes into a more effective form when it passes through the intestinal wall; in any case, it appears in the urine as an amido-compound which is characterized by pronounced fluorescence. This amido-compound possesses slight spasmolytic properties which are perhaps explained by the clinically observed antidiarrheal effect. Tests on dogs and

cats shown that in oral administration there was distinct excretion of the substance through the bile.

Besides the effect upon the murine typhus strain, the substance possesses additional, very considerable therapeutic properties. In subcutaneous and oral application it is characterized by a very pronounced effect upon general streptococcus infections, which is distinguished from the indirect effect of the sulfonamides by the fact that the streptococci are killed rapidly in vivo. Even in great dilutions it prevents the development of many types of bacteria. In tests on mice it caused, upon oral administration, spontaneous lambliosis to disappear completely.

Application in the human organism

Tolerance. Substance No. 3582 has a repulsive taste which causes sensitive individuals to vomit. In ingestion of the substance one must see to it that it does not remain too long in the mouth and that no No. 3582 enters into solution from the granular state. Thus the substance is best ingested in the dry state, and followed by much water or other beverage. It is not recommended to ingest the substance into an empty stomach, because thus possibly irritations of the mucosa by the substance might cause nausea. Healthy individuals who ingest the granulated No. 3582 observing these precautions will tolerate it as a rule for weeks without any disturbing effects. In typhus patients there may, however, occur vomiting even after correct ingestion of the substance; this vomiting is, however, probably of cerebral causation, and less connected with the substance than with the disease. Many typhus patients tolerate No. 3582 in granular form without difficulty.

Experiences with typhus patients

Already at this time substance No. 3582 has proved its worth in the treatment of typhus in a number of cases; it is especially effective in the treatment of the early stages of the disease. In general, one administers individual doses of 0.25, corresponding to one teaspoonful of the granulated substance, in consecutive intervals of 6 hrs. One course of treatment requires as a rule 6 individual doses, a maximum of 10 doses. The results of the treatment generally become evident after about 2 days. At this point in cases with pronounced diarrhea t e stools are distinctly affected. The lowering of temperature is not the result of an antifebrile effect of No. 3582, but it is a specific effect, since in experimental tests in febrile animals the substance

has no antifebrile effect. In the same sense one must also evaluate the observation that after 3582-treatment in typhus patients the lowering of the temperature takes place before the exanthem becomes pale.

If after a longer administration of #3582 there occur symptoms of stomachal irritation, or if the patient vomits a dose of the substance the 3582-therapy may be continued after a pause of a few hours. One often succeeds in stopping cerebral vomiting by administration of 0.3 gm chloretone.

3. Substance #3582 used in other diseases.

#3582 proved successful also in the treatment of Volhynian fever. In this a smaller number of individual doses will generally suffice. Because of its general chemotherapeutic properties, #3582 is suitable for the treatment of bacillary dysentary and non-specific intestinal affections. For amebas, #3582 has a specific efficacy corresponding to that of Rivanol; thus it is useful in the treatment of amebic dysentary.

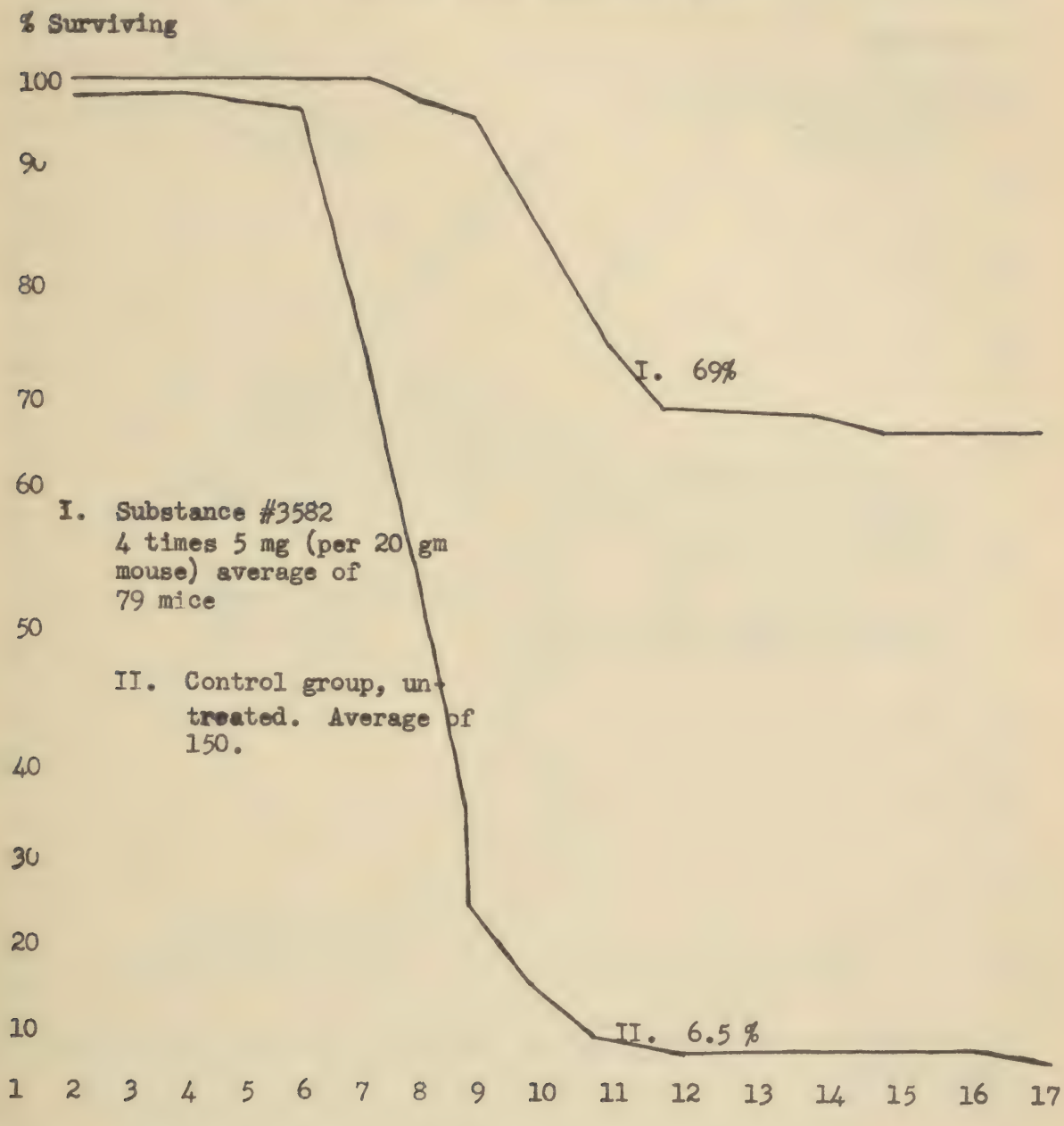
4. Form of application.

Substance #3582 is used in granular form, of which a heaping teaspoon corresponds to the customary individual dosage of 0.25. it is not to be ingested in an empty stomach. The granular substance is ingested in a dry state, and it is washed down immediately with a generous amount of liquids.

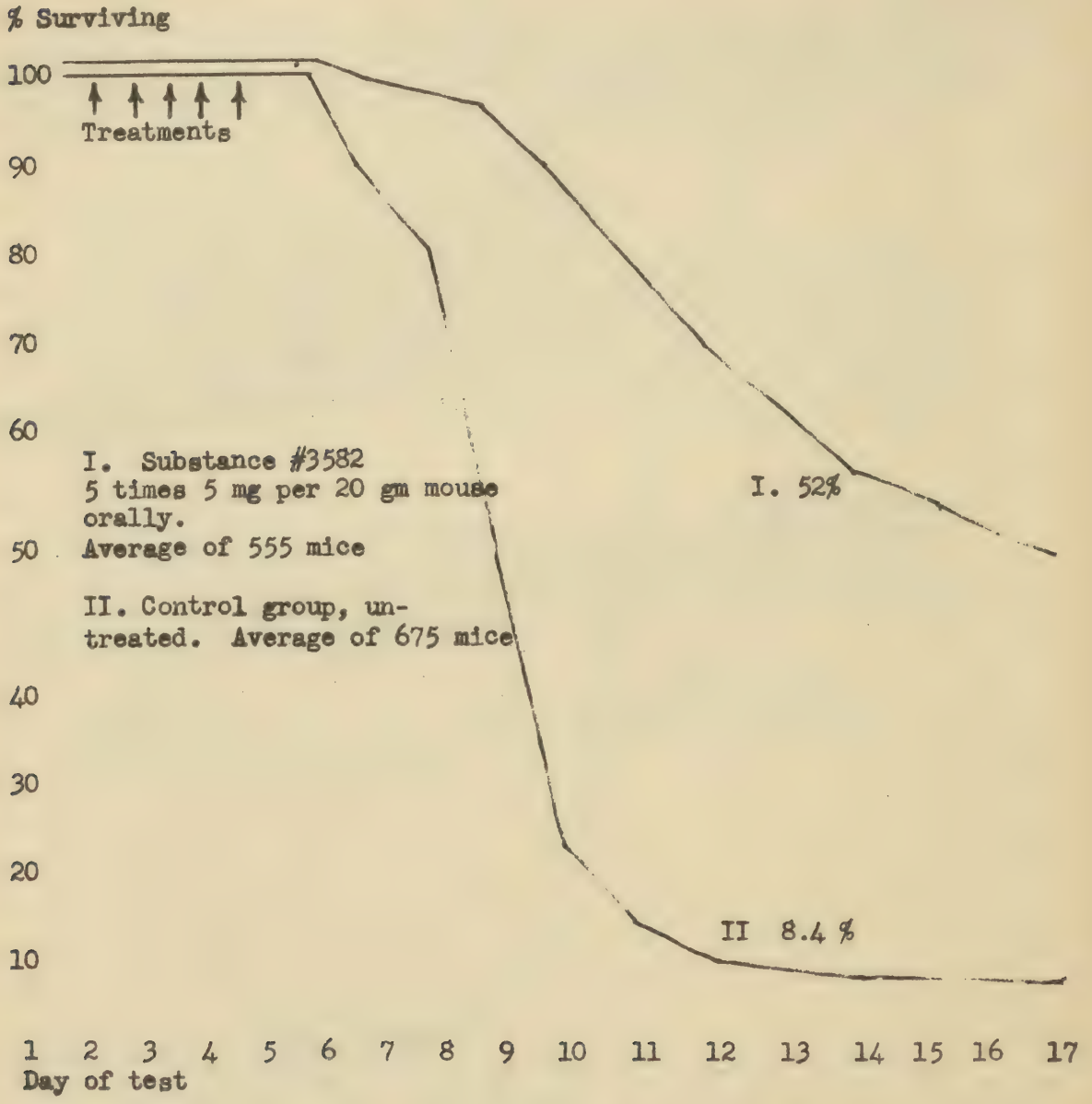
5. Packing.

Bottles containing 100 gm of the granular substance. One heaping teaspoon corresponds to 0.25 gm.

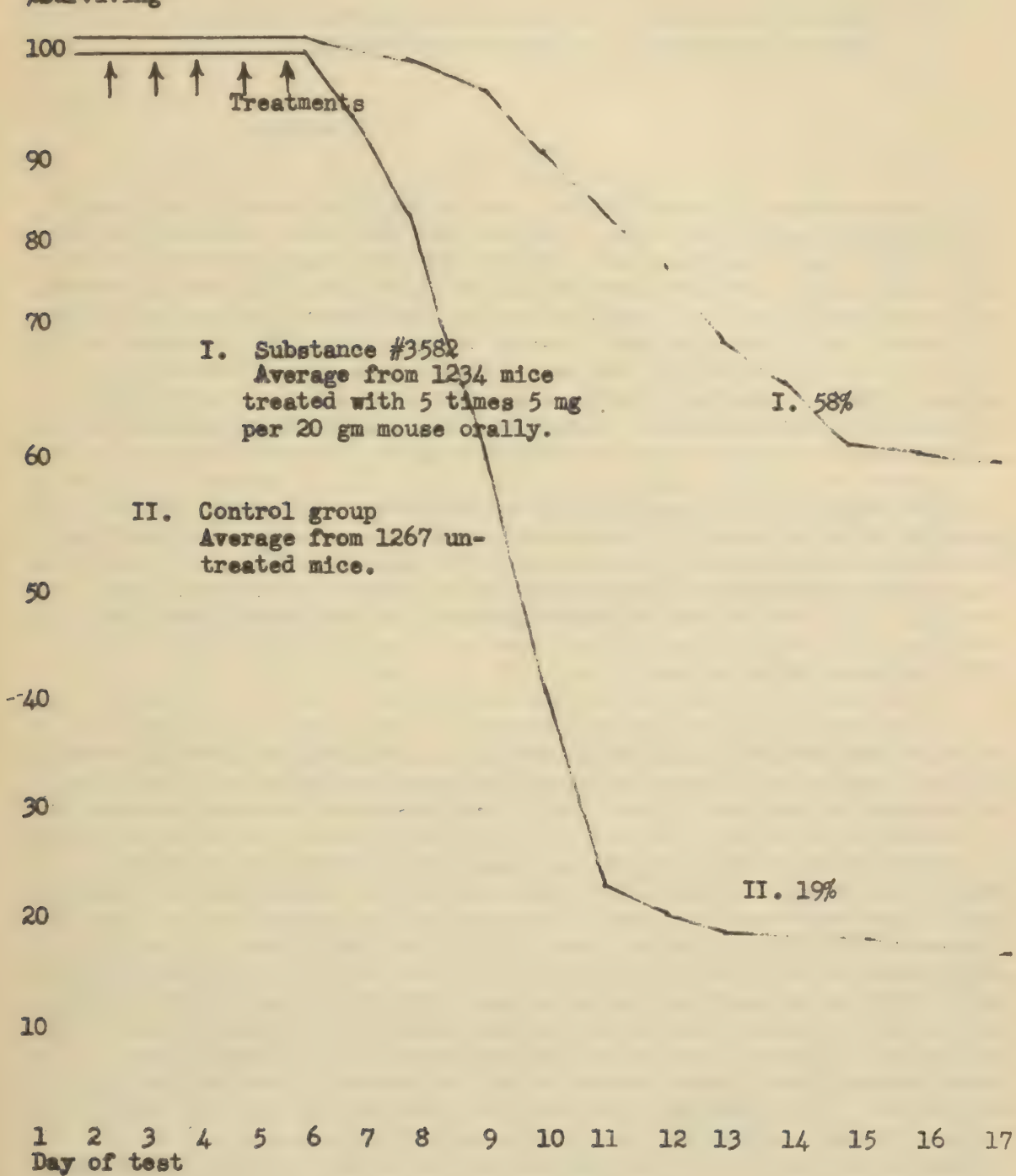
Chemotherapeutic test with mice, infected with Rickettsia Mooseri.
Surviving in % after treatment with substance #3582



Average life of mice infected with Rickettsia Mooseri and treated with substance #3582.



Chemotherapeutic effect of substance #3582 in mice infected with Rickettsia Mooseri.



APPENDIX 4

RUTENOL

I.G. Farbenindustrie A.G. Frankfurt (Main)- Höchst,
Chemisch-Pharmazeut. u. Bero-Bakteriologische
Abteilung.

R. Fussgänger.

Chemotherapeutic remedies for true typhus with specific efficacy have not been known until now. For the last 10 years systematic investigations have been undertaken for the discovery of such remedies. Above all, Otto, Wohlrab, and Schäfer have conducted extensive series of tests, but it was not possible to find anything more than just indications of an effect upon the disease in the mouse. For a causative agent, these investigators used a rickettsia-transmitted strain of Mexican typhus tabardillo fever), isolated by Mooser, on whose suitability for chemotherapeutic experimental series Wohlrab reported in 1937 at the 17th meeting of the Vereinigung für Mikrobiologie.

The danger of increased incidence of typhus occasioned by the Eastern campaign caused the author to take up very extensive laboratory experiments to discover a chemotherapeutic substance for medicinal therapy of typhus, since the manufacture of vaccines in quantities necessary for the protective inoculation of the entire military and civilian personnel in the Eastern area could not be performed even with the best organization.

Since work with the causative agent of true typhus in large experimental series is difficult and since the study of immunity conditions showed the close relationship of genuine typhus with the causative agent of Mexican typhus, the chemotherapeutic test series were performed with Mooser's strain. Extraordinarily many preparations from a multiplicity of chemical groups were tested for their efficacy by means of this model test. Above all many of the classical chemotherapeutic remedies were examined; in most cases they proved to be totally ineffective. Certain indications of an effect were found in oral administration of some arsinic acids. In the further course of these large-scale experiments a substance was found which has a very regular, strong influence upon the course of the disease in regard to intensity and lethal outcome, and in the application of which a very large percentage of the infected experimental animals were kept alive and were cured. This substance is No 3582, in entensive clinical tests in genuine typhus, Wolhynian fever, and other rickettsioses. It is a nitroacridine derivative of complicated structure. A further intensification of the effect was obtained by the combination of the base of substance 3582 with an arsinic acid. Rutenol is a salt from the

3582- base with this arsinic acid, and it has been used since in clinical tests.

Toxicology:

Rutenol is only slightly toxic. The dosis tolerata maxima is per kg mouse 0.5 gm with subcutaneous and 1.5 gm in oral administration. Rabbits tolerate 35 mg per kg intravenously.

Chemotherapeutic data:

For biological tests of the new typhus remedy on the causative agent of Mexican or murine typhus, mice were used in large test series, as experience had shown that uniform results can only be obtained if each preparation. each individual dosage, and each manner of administration (subcutaenous, oral, intravenous) are applied to as large a group of mice as possible, in order to reduce the biological stray results occurring in this infection to a minimum. For the infection of the series of mice, the author used the emulsified brains from gravely diseased passage animals, in certain dilutions, which caused a 90 - 100 % mortality in the untreated control animals. In spite of frequent adjustment of the optimal dilution of the emulsified brains there appear fluctuations in virulence, which render the determination of effective remedies difficult. After the basic substance, namely preparation #3582, had excelled time and again in all tests, the author began in all large-scale tests to treat a collective group with this substance, in addition to the untfeated control animals, and thus he was able to determine the degree of efficacy of a new substance in comparison with No. 3582 as a standard substance.

The aspect of the disease in intraperitoneally infected mice had approximately the following course: On the 4th or 5th day after infection the first symptoms of the disease became visible. They were a lack of motion and raised fur; as the disease continued, there appeared uni- or bilateral conjunctivitis, and extensive edemas developed in the head of the animal. Before death occurred -- generally between the 8th and 10th day of the test -- the author observed occasional symptoms of paralysis, and frequently diarrhea and spasms. While the mice in the control series had, with very few exceptions died by the end of the 10th day of the test the disease in the majority of the animals treated with substance # 3582 orally had a distinctly milder course. In most instances these animals did not even show any symptoms while the control animals already displayed very grave symptoms of disease. Lack of motion and raised fur appeared several days later. Many mice recovered very rapidly from this condition. Only a part of the experimental animals suvvumbed to the infection, howecer much later than the control animals.

From a juxtaposition of the percentages of the mice surviving every day of the experiment it was possible to obtain a standard for determining the efficacy of a preparation. The best result was obtained by oral administration of #3582 for a period of several days.

The greatest number of survivals was obtained with 5 times 5 mg per 20 gm mouse, administered orally. With smaller daily doses the effect was smaller, likewise the substance appeared less effective in sucutaneous and intraperitoneal application, evidently because of the greater toxic effect in this type of application.

The use of # 3582 as standard substance in almost all test series made it possible to calculate the average course of the disease in treated and untreated mice from a very large number of experimental animals, and to present it in an unequivocal curve. In this the control animals participating in the same large-scale experiment were contrasted with the series treated with substance #3582. The curve depicting this represents the average of 675 mice infected with rick ettsias but not treated with any remedy (control animals). Contrasted to this is the curve of 555 mice which all had received at least the standard dosage of 4, but most mostly 5 times 5 mg substnace #3582 orally. While of the control ani als only 8.4% survived the infection by the end of the 17th day of the experiment, in 31 large-scale experiments with #3582 an average of 52% of the experimental animals survived, in spite of the fluctuations in virulence. Extension of the period of observation hardly changes this quotient at all; on the other hand the juxtaposition of the two curves shows that a premature interruption of the experiment on about the 10th or 11th day and an evaluation based thereon leads to an overestimation of the efficacy of the substances tested.

After it had become evident that experimental typhus may also be influenced effectively by some arsinic acids, the author began to produce a series of arsinic acid salts of the basic substance #3582, which was found to be so effective, and to compare them with the latter. These tests were conducted in such a manner that in the experiment always the same parts of the nitroacridine base of substance##3582 were administered with the corresponding quantities of the arsinic acid, in order to compare quantitatively the increase of the effect by the addition of the arsenic acid. One of the most effective of the arsinic acid salts received the name "rutenol". It contains about 50% of the nitroacridine base. The added curve shows for comparison, besides the course of the experiment in the untreated controls and in those treated with standard preparation #3582 the curve No I which is the average of several experiments with rutenol (5 times 10 mg orally per 20 gm mouse) from 115 mice. According to this curve on the 10th day of the experiment still 96% of the experimental animals were surviving, whereas only 25% of the control animals remained alive at that time. For the 17th day of the experiment the corresponding numbers were 71 % with rutenol and 8.4 % with the control animals. From this curve it is seen that there is a most considerable influence upon the experimental typhus infection. This result represents a great success, in consideration of the many chemotherapeutic tests in experimental typhus, which nearly always had a negative course; this success justifies the clinical testing of the application of rutenol in true typhus.

Work on clarifying the mechanics of the effect of this substance is in full progress. It must be assumed that rutenol when passing through the intestinal wall is changed to a more effective form. The nitroacridine component reappears in urine as an amido-compound characterized by pronounced fluorescence. This amido-compound possesses weak anti-spasmotic (?) spasmolytic properties, probably explained by the clinically observed antidiarrheal effect. In oral administration, tests performed with dogs and cats showed a distinct excretion through the bile.

Besides the effect upon the murine typhus strain, rutenol possesses very considerable additional therapeutic properties. In subcutaneous and oral administration it is characterized by a powerful effect upon general streptococcus infections, which is distinguished from the indirect effect of the sulfonamides by the fact the streptococci are rapidly killed in vivo. Further even in greatest dilutions it possesses the property of impeding the development of numerous bacteria. In experimental tests on mice it causes, in oral administration, spontaneous lambliosis to disappear completely.

Application in the human organism.

1. Tolerance.

Healthy individuals tolerate rutenol without any disturbance of their well-being. In patients with gastric disease and also in patients with grave typhus cases it amy, especially in continuous application, lead to irritations of the gastric wall; thus it is recommended that the substance never be ingested into the empty stomach and always be-washed down by means of some beverage, soup, or oatmeal, and if necessary one-half to one day of intermission is to be interpolated in the course of therapy.

2. Experiences with typhus patients.

Rutenol has already proved its worth in the treatment of typhus in a number of cases and it seems to be especially effective in the early stages of the disease. Success of the treatment is generally preceived after 2 days. At this point, a distinct effect also is noticed in the stools of cases with pronounced diarrhea. The decrease in fever is not the result of an antifebrile effect of rutenol, but it is a specific effect, since rutenol in experimental tests in febrile animals did not have an antifebrile effect. In the same sense one must evaluate the observation that after rutenol treatment the lowering of the fever in typhus patients takes place before the disappearance of the exanthema.

In general one administers individual doses of 0.4 gm continually in 6 -hr. intervals. If that is not possible one may administer the same dose three times daily. A cure requires as a rule 6 - 10 individual doses.

If after longer administration of rutenol there occur stomachal irritations, they manifest themselves by the fact that the patient vomits the substance. However, there is no further injury to the patient. In the animal experiment even with large over-dosage rutenol never causes a recognizable injury of the gastric and intestianl mucosas. Thus there should be no hesitations to continue the administrations of rutenol as long as the symptoms of stomachal irritation can be overcome, possibly by some pause in the treatment.

3. Rutenol in other diseases.

Rutenol also proved successful in the treatment of Wolhynian fever. Here as a rule a smaller number of doses will suffice. Because of its general chemotherapeutic properties rutenol is also suitable for the treatment of bacillary dysentery and non-specific intestinal affections. Toward amebas rutenol has a specific effect of the type of that of rivanol and it is thus also useful for the treatment of amebic dysentery.

4. Forms of application.

Rutenol is used in form of a 5% granulate, of which 2 teaspoons correspond to the custmmary individual dose of 0.4 gm. Rutenol is not to be ingested into an empty stomach; it is best administered in combination with oatmeal, soup, or some beverage. It must be pointed out expressly that sympto s of stomachal imcompatibility are exceptional cases and that they, due th their harmless nature, in no wise exclude the continuation of the treatment after some interruption.

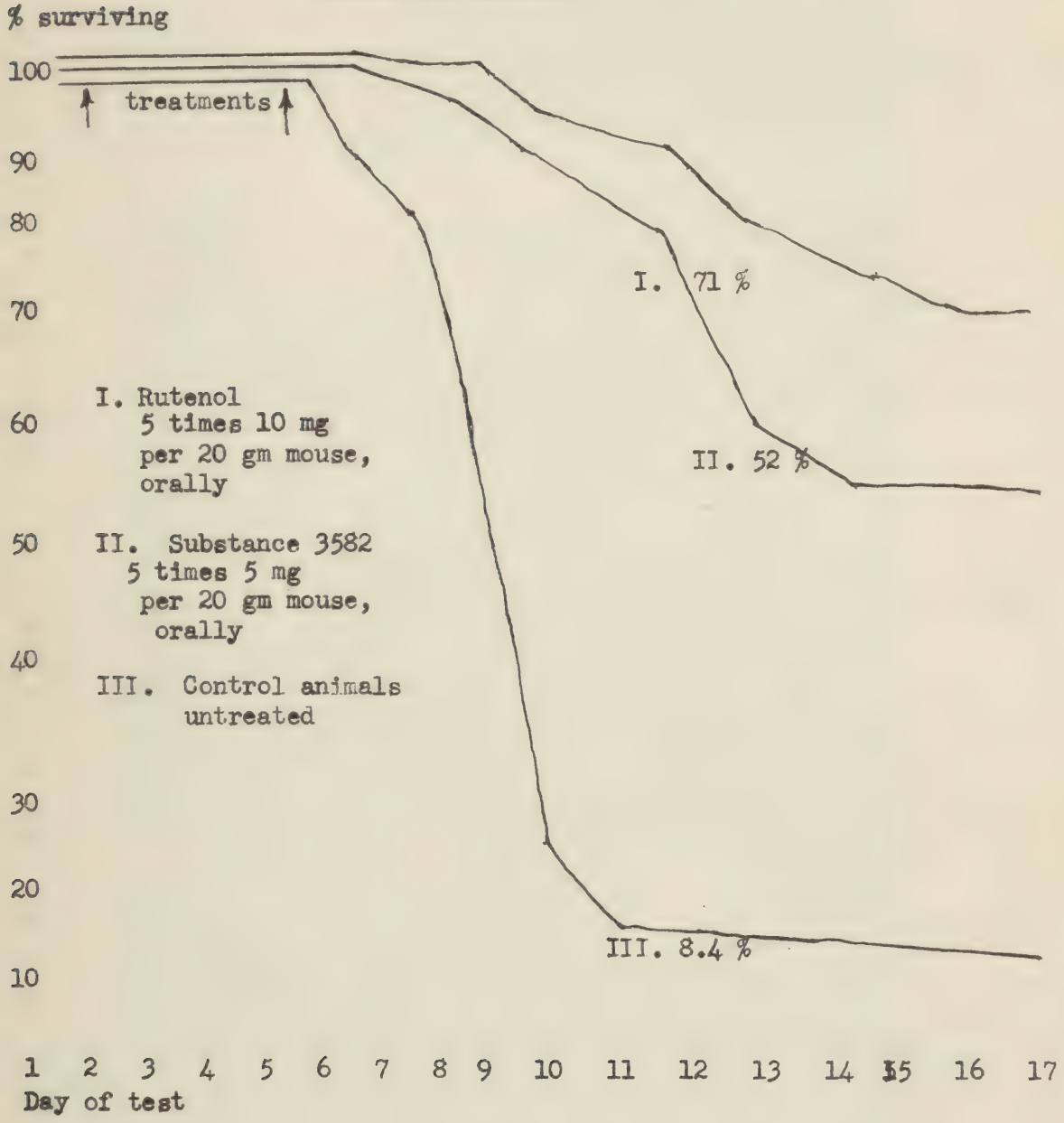
5. Packing.

Bottles containing 100 gm of the granular substance.
Two teaspoons of granular substance equal to 0.4 gm.
Parenteral rutenol therapy:

Rutenol is not to be administered intramuscularly and subcutaneously, as it causes very great irritations in the tissues. Also the intravenous injection of aqueous solutions causes difficulties as very great dilutions must be chosen to avoid vascular thromboses. However, if one applies rutenol in solution with 25 % alcohol addition, there generally appear no injuries to the veins, so that the author recommends for intravenous injections an alcoholic special solution which can easily be prepared by means of an iso-double-ampule.

Rutenol is injected intravenously in the dosages of 0.1 - 0.25 daily or three times per week. Since in wartime conditions the acquisition of iso-double-ampules for the 0.25 dosage is difficult, the preparation is issued in a dry-ampule with foot, into which the contents of the accompanying ampule of solvents is injected. In this manner one obtains the solution ready for use in intravenous injection.

Comparison of the chemotherapeutic effect of rutenol with that of substance 3582 in mice infected with Rickettsia Mooseri.



A P P E N D I X 5

Photographs of I. G. Farben Headquarters, Frankfurt a. Main, and of the Höchst Plant.

I. G. HEADQUARTERS, FRANKFURT a. MAIN

I. G. HEADQUARTERS, FRANKFURT a. MAIN

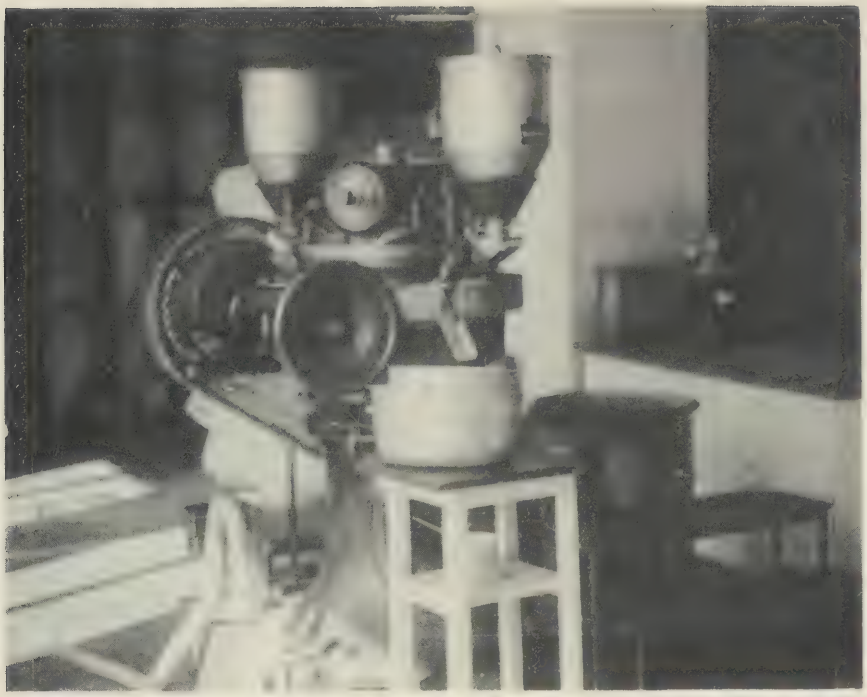
I. G. HEADQUARTERS, FRANKFURT a. MAIN

HÖCHST PLANT - STREET VIEW

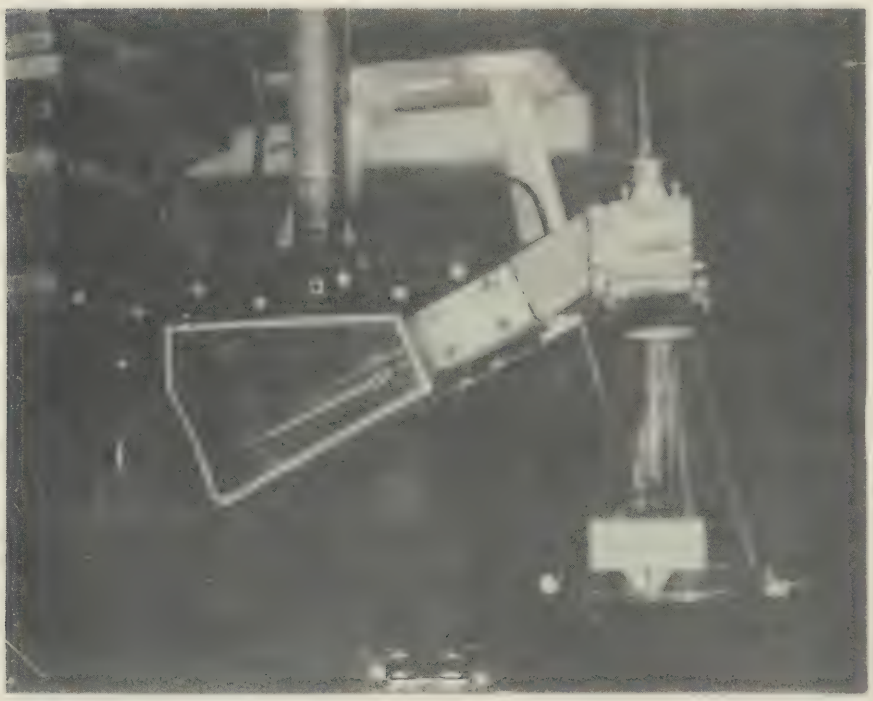
HÖCHST PLANT

HÖCHST PLANT

HÖCHST SEMI-COMMERCIAL LABORATORY



HÖCHST TABLET MACHINE



HÖCHST SALVARSAN FILLER